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IMMEDIATE OUTCOMES OF TREATMENT OF SEVERE MITRAL ANNULAR CALCIFICATION

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Mitral annular calcification (MAC) is a chronic degenerative process involving the fibrous part of the mitral complex, characterized by calcium deposition and loss of valve function. MAC prevalence is 8–10%, but despite this, the clinical significance of MAC is underestimated. Currently, there are reports that complete decalcification leads to improved long-term outcomes in patients with severe MAC. An analysis of the immediate outcomes of mitral valve surgery in patients with severely calcified mitral annulus with decalcification was performed. The calcified annulus fibrosus underwent complete decalcification in all cases. Calcium deposits were removed in a single block, in 6 cases it was reconstructed with a xeno-pericardial patch; in 2 cases the annulus fibrosus was sutured. There were 2 cases of in-hospital mortality, caused by acute heart failure on day 8 in 1 patient and pulmonary embolism on day 30 after operation in the second patient. There were no complications associated with coronary artery injury and left ventricular posterior wall rupture. Experience in the treatment of severe mitral valve calcification with extensive annulus fibrosus decalcification and subsequent reconstruction is possible and gives satisfactory results.

Keywords: heart base calcification, radiation therapy, decalcification.

INTRODUCTION

Calcification of the base of the heart is a progressive degenerative process characterized by calcification of the fibrous skeleton of the heart with involvement of the mitral annulus and the surrounding myocardium, which may eventually lead to loss of valve function. Multiple studies have shown that there is a high prevalence of this disease in clinical practice, ranging from 7% to 24%. In a series of 258 autopsies, the overall incidence in persons over 50 years of age reached 8.5%; a higher prevalence is found in older women, which reaches 43.5% by the age of 90 years [1].

Systematic retrospective, echocardiographic studies have shown that severe calcinosis is closely associated with age, atrioventricular valve regurgitation, and aortic valve stenosis. Mohammad et al. retrospectively reviewed 24,380 echocardiograms and found that severe mitral annulus calcification was present in 11.7% of patients with mitral regurgitation [2]. Improvement of highly sensitive diagnostic methods used in clinical practice made it possible to estimate the prevalence of this pathological condition. A study by Allison et al. based on CT scan in asymptomatic patients revealed that 8% were found to have mitral annular calcification and suggested that the calcification may be of atherosclerotic nature [3]. Severe mitral valve calcification can serve as a marker for structural changes in the heart, with increased risk of cardiovascular disease and sudden cardiac death [4].

Population aging, leading to an inevitable increase in risk factors (arterial hypertension, diabetes mellitus, kidney disease) [5], and use of radiation treatment for thoracic tumors will significantly increase the prevalence of severe mitral valve calcification in the future, and as a consequence, lead to complex changes in the patient population, creating additional problems in the treatment of this condition. Surgical treatment of patients with valve disease combined with annulus calcification is associated with high in-hospital mortality and postoperative complications. To prevent postoperative surgical complications, surgical treatment of severe calcification requires additional complex procedures. Techniques involving complete decalcification and reconstruction of the mitral valve annulus described in the mid-1990s have not lost their relevance at the present time and are the most preferred surgical techniques that would avoid severe postoperative surgical complications [6, 7].

Objective: to evaluate the immediate outcomes of surgical treatment of severe mitral valve calcification with complete decalcification in a single block and reconstruction of the annulus fibrosus.

MATERIAL AND METHODS

The study enrolled 8 patients operated on from 2016 to the present with severe mitral annular calcification. The mean age of the patients was 64.12 ± 10.57 (47–80 years), all patients were female and had NYHA heart failure functional class 3–4. Most of them had va-

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rious comorbidities aggravating the course of the underlying disease. The mean logistic EuroScore II risk score was 9.73 ± 4.49% (ranged widely from 3.07 to 15.66%), the 30-day Society of Thoracic Surgeons Predicted Risk of Mortality (STS PROM) was 8.96 ± 6.93% (ranged from 3.99 to 21.26%). In 2 patients, the operation was repeated, 1 patient had undergone 2 years earlier mitral valve repair with Sorin 29 mechanical prosthesis, De Vega tricuspid valve plasty and Labyrinth operation for mitral valve prolapse and persistent atrial fibrillation, the present hospitalization was for paraprosthetic fistula. The second patient, 13 years earlier, underwent mitral valve repair with Carbomedics 29 mechanical prosthesis, Boyd tricuspid valve plasty for rheumatic lesion. Her return visit to the hospital was due to aortic stenosis and mitral prosthesis dysfunction – increase in pannus with formation of mitral stenosis.

Four patients had rhythm and conduction disorders: 2 had permanent atrial fibrillation, tachysystolic variant, 1 had third-degree atrioventricular (AV) block, for which a permanent pacemaker was implanted, 1 had an incoming AV block, Mobitz type I.

Transthoracic echocardiographic examination was performed on Phillips iE 33 (Philips Medical Systems, Andover, MA). In addition, visualization of cardiac structures, hemodynamic characteristics of the valves were calculated, and ventricular function was assessed. To visualize the mitral annulus and assess the extent of annulus fibrosus calcification, the study was performed from parasternal access along the short axis. Grade 3–4 mitral regurgitation was revealed in 4 patients (50%). Mitral stenosis in 6 patients (75%), mean values of peak and mean diastolic gradients on mitral valve were 19.33 ± 8.09 and 9.8 ± 7.19 mmHg. Aortic valve stenosis in 4 (50%) patients, mean peak and mean systolic gradients were 103.25 ± 12.57 and 74.75 ± 15.73 mmHg, and combination with aortic valve insufficiency in 2 (25%) patients. Relative tricuspid regurgitation requiring surgical correction was detected in 1 patient (12.5%). The functional state of the left ventricular myocardium was in satisfactory condition, the mean value of left ventricular ejection fraction was 67 ± 10.7%. Changes in left ventricular geometry in the form of eccentric hypertrophy were observed in 3 patients, with an EDV/BSA ratio of 70.3 ± 33.4 mL/m^2, (79 to 137.5 mL/m^2). The mean pulmonary artery pressure by measuring the tricuspid regurgitation rate in continuous-wave Doppler ultrasound was 55.25 ± 13.9 mmHg.

All patients underwent computed tomography (CT) scan. Calcification was defined as a particle with density of ≥200 Hounsfield units (HU). Calcium levels (3259.5 to 7383.18), calcium volume in the fibrous ring (1005.1 to 2222.82 mm^3), weight (2725.6 to 6014 mg), and extent of calcification expressed in degree of the arc involved (62 and –331 degrees) were calculated based on the slices. Calcium was quantified according to the method described by Agatston et al. [8].

All patients underwent coronarography. Right coronary artery (RCA) dominance was observed in 6 patients, left coronary artery (LCA) dominance was noted in 1 patient, and balanced circulation was observed in 1 patient. Coronary artery lesions were detected in 1 patient (right coronary artery of the proximal third 85%, posterior interventricular branch of the right coronary artery 80%, circumflex branch 75%). Additional clinical characteristics of the patients are presented in Table.

SURGICAL TECHNIQUE

In all cases, access was performed through median sternotomy with cardiopulmonary bypass (CPB) by cannulating the vena cava and ascending aorta with hypothermia 28 °C. Cardioplegia in isolated mitral correction was performed in an antegrade manner into the aortic root; with interventions on the aortic valve, it was performed selectively into the coronary artery orifices. The mitral valve was accessed through the vertical bicuspid access. Complete decalcification was performed by opening the fibrous tissue over the decalcification; calcium was removed in a single block throughout the acute route, between 2 fibrous triangles. After decalcification, a defect was usually formed completely separating the left atrial myocardium from the ventricle. In 2 cases,

Table

Clinical characteristics of patients (n = 8)

Body surface area (kg/m^2)	1.80 ± 0.18 (1.57–2.16)
Diabetes (n)	3
CKD-EPI creatinine clearance (mL/min/1.732 m^2)	72.25 (50–109)
Stage 3 CKD	3
Chronic obstructive pulmonary disease (n)	3
Hypothyroidism (n)	2
Arterial hypertension	6
Stroke	2
Etiology degenerative / endocarditis* / RILI / rheumatism	3/1/2/2

* – endocarditis was secondary to degenerative changes in the mitral valve.

the annulus fibrosus was repaired by suturing the formed defect, in one case with a mattress-twisted stitch with 4-0 monofilament, and in the other case with 6 vertical figure-of-8 sutures with 2-0 braided sutures. In 6 cases, the mitral annulus fibrosus defect was closed by closing the atrioventricular junction defect with a xenopericardial patch (manufactured by Bakulev Scientific Center for Cardiovascular Surgery, Moscow) of various sizes. Xenopericardium was implanted in 5 cases with 4-0 continuous monofilament prolene sutures in one row. In the first case, the lower edge of the patch was fixed to the left ventricular myocardium with 12 U-shaped sutures on Teflon spacers (this maneuver was performed due to the large size of the defect and the 8 × 1.5 cm patch for more reliable fixation of the latter). The upper row of the flap was fixed to the edge of the left atrial wall defect.

In all cases, the severed posterior mitral valve leaflet was captured in the prosthetic suture; in the patient with infective endocarditis, the anterior leaflet in the area of commissures. The prosthesis was implanted with

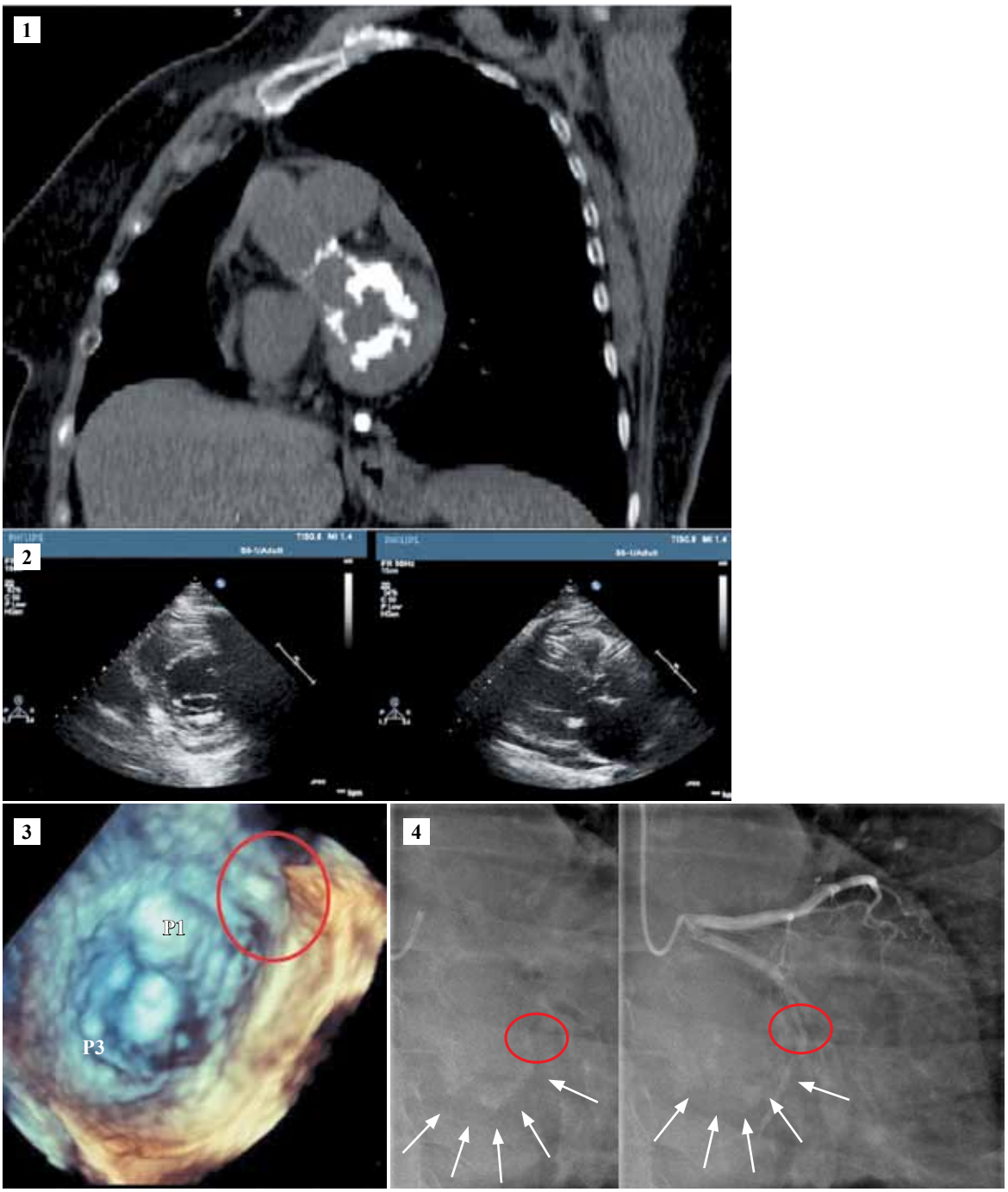

Fig. 1. Computed tomography: 1 – Chest MSCT; 2 – echocardiography, longitudinal and cross-sectional parasternal access; 3 – 3D reconstruction of the mitral valve; 4 – coronary angiography (arrows show mitral annulus calcification, the circle indicates the possible location of coronary artery lesion)

U-shaped sutures with spacers, so that in the projection of the native annulus fibrosus, the sutures were applied intraannularly, and in the area of annulus fibrosus reconstruction, the sutures were applied supraannularly behind the central part of the xenopericardial patch.

Additional surgical procedures were performed in the following volume: aortic valve prosthetics in 4 (50%) patients (mechanical n = 4), subcommissural suture annuloplasty of the aortic valve with suturing of the left atrial auricle from the inside in 1 patient, plastic surgery, Morrow myectomy in 1 patient.

RESULTS

The mean CPB time was 258 ± 58.89 minutes, the mean aortic clamping time was 152.25 ± 41.58 minutes. The mean reperfusion time was 105.7 ± 37 minutes.

Mechanical prostheses of different sizes were implanted in the mitral valve position: Carbonix MDM 26 in 1 case, MDM prostheses size 28 in 4 cases, Medtronic 27 prosthesis in 1 case, Medtronic 31 prosthesis in 1 case, biological prosthesis BiolAB 31 in 1 case.

Two (25%) patients died in the early period. One case was associated with the development of acute heart failure followed by multiple organ failure. The second case of in-hospital mortality was associated with pulmonary embolism on day 31 after surgery in an obese patient (BMI 43.28 kg/m^2) who underwent prolonged ventilation (619 hours of mechanical ventilation) for acute stroke, after being transferred to the general ward.

The mean time spent in the intensive care unit was 128 ± 204.81 hours (19 to 619 hours). In the early postoperative period, there were 3 cases of prolonged ventilation (more than 72 hours) associated in 1 case with acute heart failure; in 1 case, there was impaired cerebral circulation, in 1 case there was neurologic deficit.

There were no cases of coronary artery injury, hemorrhage and left ventricular posterior wall rupture. Among nonlethal complications, hydrothorax was the most common – in 4 patients. There was one case of third-degree AV block, for which a permanent pacemaker was implanted, as well as 1 case of pericarditis with the development of cardiac tamponade.

Mean hospital stay was 18.8 ± 12.6 days (7 to 42 days). At the time of discharge, the functional status of the patients had significantly improved (NYHA class 1–2). The mean diastolic gradient at the mitral valve was up to 5.6 ± 1.4 mmHg, peak 10.5 ± 3.4 mmHg. The indexed left ventricular end-diastolic volume was 62.7 ± 20.6 ml/m^2.

DISCUSSION

Currently, the strategy for surgical treatment of mitral valve defects complicated by severe mitral annular calcification can be divided into several types. A less aggressive approach to calcified annulus fibrosus involves intra-atrial fixation of the prosthesis behind the atrial myocardium. Nataf et al. used this technique in 21 patients, but the results were unsatisfactory, 1 case of hospital mortality. due to atrial wall rupture in a patient

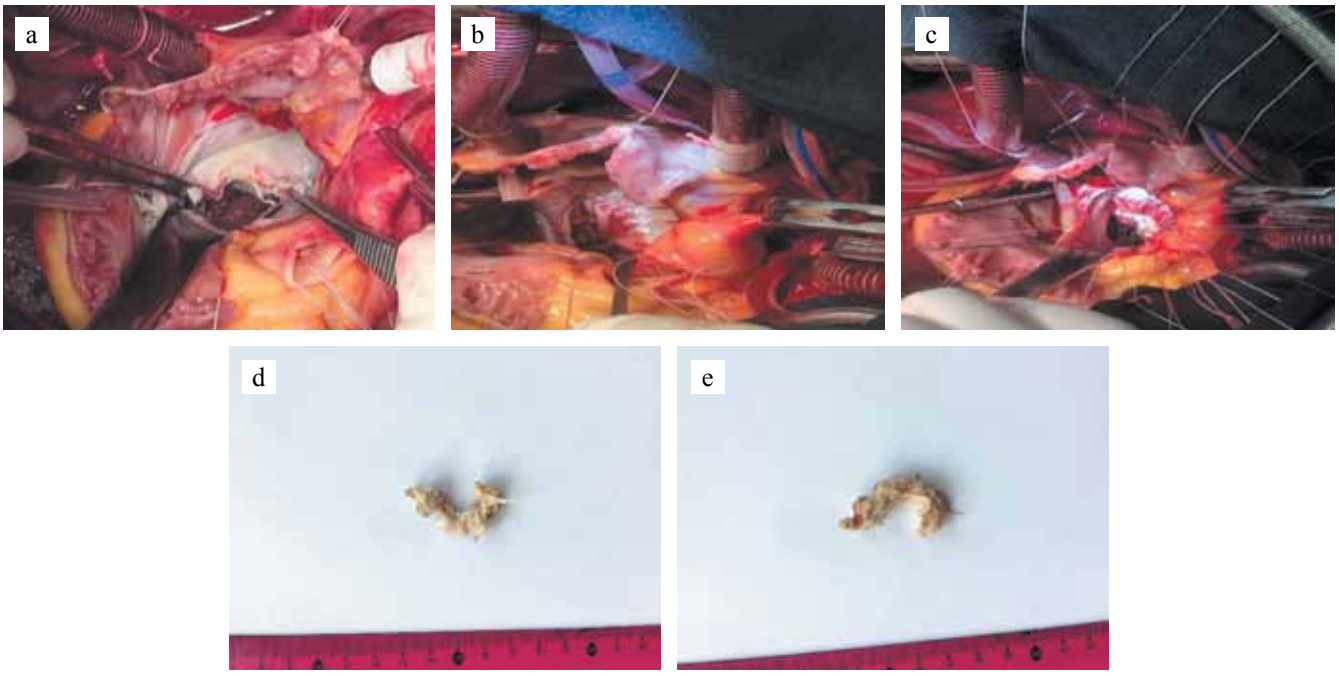

Fig. 2. a – Mitral valve exposure, base calcification in the posterior mitral leaflet projection. b – Pericardial patch plasty after complete decalcification. c – U-shaped prosthetic sutures on spacers. d, e – excised annulus fibrosus calcium from ventricular and atrial surfaces

with renal failure on hormonal therapy and 4 cases of paraprosthetic fistulas [9].

Hussain C.T. et al. suggested limited debridement of the calcified annulus with creation of a 1.5-cm wide polytetrafluoroethylene (PTFE) felt washer in between the annulus and sewing ring of the prosthesis from trigone to trigone posteriorly. The valve and the washer are tied down. The washer is then sutured to the atrial wall with a second suture line (n = 20). This "sparing" decalcification technique ensures prosthesis implantation with a low risk of ventricular rupture. One case of hospital mortality was associated with the initial severity of the patient. The authors noted the absence of paraprosthetic leaks and repeated interventions. The only serious limitation of this technique is its use in patients with wide annulus, as it results in significant reduction in the annulus fibrosus size [10].

Another method of surgical treatment of the pathology, avoiding direct manipulations with calcified fibrous rings, is creation of a bypass anastomosis between atrium and left ventricular apex with a valve-containing conduit. This concept is not new, it has been adopted from the arsenal of mitral valve atresia treatment [11]. The technique can be used as an independent option; severe mitral valve regurgitation is a limitation preventing wide application of this technique. Creation of bypass anastomosis may be safer than standard mitral valve replacement in severe patients with concomitant lesions of other valves and heart structures. However, due to small number of observations and absence of long-term results, careful study is required [12].

Within a little more than a quarter of a century since a solution to this problem was described, at least 3 different methods aimed at complete decalcification with subsequent restoration of the integrity of the annulus fibrosus of the mitral valve have been proposed. The methods described by Carpentier and David are the most widely used in clinical practice for annulus fibrosus reconstruction after complete decalcification. Both methods are aimed at restoring the integrity of the posterior hemisphere of the annulus fibrosus after complete decalcification; in the first case, reconstruction is performed by suturing the edges of the defect; in the second case, pericardial patch is used. Both methods have proven satisfactory and show comparable results. Depending on the depth of calcium deposition, this maneuver may result in injury to the obturator artery in the lateral commissure, and the AV node in the medial commissure projection. The fact of type-1 left ventricular rupture is also important. NG C.K. and colleagues demonstrated the experience of surgical treatment of severe annular calcification in 21 patients using both methods in isolated mitral valve surgery; freedom from reoperation by the 5th year of follow-up was 94.5% with 100% survival [13]. In contrast, Uchimuro T. and colleagues from the University of Tokyo reported 6.6% hospital mortality in 61 patients, including rupture from pseudoaneurysm in a 93-year-old patient on day 80 after surgery. It is worth noting the advanced age of the patients, whose average age was 70 years; almost half of the patients underwent aortic prosthetics in addition to mitral valve intervention. Sudden cardiac death dominated the structure of the cardiac mortality in the mid-term follow-up in 6 out of 12 cases. One patient underwent reoperation 6 years after operation due to paraprosthetic fistula.

Multiple comorbidities that reduce the functional reserve necessary for recovery after surgery classify this pathology as a systemic disease, which is expected to increase the risk of postoperative mortality and complications. A recent retrospective, multicenter study identified several key points. First, patients who underwent surgery with mitral valve ring calcification had a high mortality rate (5.8%); there was also a high rate of postoperative complications in the form of repeated reoperation for bleeding, acute kidney injury requiring dialysis, and prolonged stay on artificial ventilation. A correlation between in-hospital mortality and number of surgeries performed was revealed. Clinics with fewer than 50 operations a year had a higher hospital mortality rate [14]. The authors attribute these results to the high initial severity and complexity of surgery. Patients with calcification were much older, had high levels of diabetes mellitus and hypertension. In addition, the study confirmed the relationship of mitral annulus calcification with prior radiation therapy. A retrospective study of surviving patients who received radiotherapy and combined chemotherapy for childhood cancer showed a high cumulative incidence of cardiovascular complications, including abnormal calcium deposition in the annulus fibrosus [15].

Operative mortality in previous studies ranges from 6 to 20% [16–19]. However, most of these studies are single-center and performed on small groups of patients. Due to the lack of a unified classification and strategy regarding operative tactics, direct comparison of results is not reliable. Studies with high surgical mortality included patients with concomitant surgical procedures on other valves and coronary arteries. Another significant risk factor influencing early mortality and survival is mitral valve replacement. A recent study compared the outcomes of surgical treatment (prosthetic versus reconstructive) in octogenarian patients, which found mitral prosthetics to be an independent predictor of 90-day mortality (31.6% versus 18.9%; $p = 0.01$) and was associated with decreased survival at 1, 3, 5 years (71 ± 3%, 61 ± 4% and 59 ± 4% versus prosthetic outcomes with 56 ± 5%, 50 ± 6%, and 45 ± 6%) [20].

A team of authors from the Mayo Clinic (Rochester, Minnesota), systematized mitral valve calcification to determine treatment strategies. The authors identified

3 degrees of annulus fibrosus damage. The mild degree corresponds to localized areas of calcium deposition or an arc of circumference limited to 180 degrees. Such calcifications in our practice were quite common, including in patients who had undergone radiation therapy, as a rule, trivial methods were used for implantation of prosthesis. Medium calcification is defined as dense, continuous calcification occupying 4/3 of the circumference. And the most severe degree of calcification occupies almost the entire annulus fibrosus with transition to the left ventricular wall and subclavian structures. This category of patients belongs to the category of inoperable patients [21].

Over the past decades, endovascular methods of treatment have evolved tremendously; now the third generation of transcatheter prostheses has appeared, allowing them to be successfully used in clinical practice. If in the aortic position, these devices are firmly established as a surgical option and the results are close to the traditional method of treatment; in the mitral position, the results remain unsatisfactory. By 2019, just over 300 different transvalvular devices were implanted in the mitral position with a 30-day mortality of 13.6%. However, this study did not include patients with severe annulus fibrosus calcification [22]. On the contrary, the experience of treating patients with severe calcification in a series of 116 patients was associated with high mortality, 30-day mortality reached 25%. By the 1st year, the survival rate was 46.3% [23].

CONCLUSION

Despite the initial severity of patients, complete decalcification followed by restoration of the integrity of the annulus fibrosus is a relatively safe and technically reproducible method. Both reconstruction techniques showed satisfactory outcomes, without occurrence of left ventricular posterior wall rupture, fatal bleeding, or coronary artery injury. Further gathering of material with long-term assessment is required.

The authors declare no conflict of interest.

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